

**REMARKS**

Claims 55 to 72 are pending and under examination in the present application. Claims 56 to 59 and 61 to 65 have been withdrawn from consideration as being drawn to a nonelected invention. Claims 55, 60, and 66 to 62 have been rejected.

Claim 55 has been amended to recite “determining the expression level of a nucleic acid.” Dependent claims 67 to 71 have been amended to be consistent with the language in amended claim 55. Support for these amendments can be found in the specification, for example, at page 33, lines 1-3. In addition, the language regarding a “nucleotide sequence” in claim 55 has been omitted to clarify the scope of the claim. Thus, there is no issue of new matter with respect to the amended claim.

Cancellation and amendment of the claims is made without prejudice, without intent to abandon any originally claimed subject matter, and without intent to acquiesce in any rejection of record. Applicants expressly reserve the right to file one or more continuing applications hereof containing the cancelled or unamended claims.

**I. Elections and Restrictions**

Applicants affirm the election with traverse of Group V, which corresponds to claim 55 and the further election of SEQ ID NO: 4758.

Applicants acknowledge that the Examiner has made the restriction requirement final. However, since Applicants traversed the initial restriction requirement, Applicants have the right to file a Petition from a Restriction Requirement under 37 C.F.R. 1.144 at a future date.

Applicants reiterate their frustration that the Examiner has only searched one sequence for the present application. By restricting the present application to one sequence, the Examiner is forcing Applicants (a small start up company with limited resources) to incur the expense of filing 9 divisional patent applications. This will generate more work for the USPTO and place undue

financial burden on applicants. This practice is neither productive nor efficient. Applicants urge the Examiner to reconsider his position and search the 9 remaining groups. At the very least, the Examiner is urged to search at least 3 additional sequences. Such sequence searches when done on the internet cannot be viewed as burdensome or excessive. Applicants reserve the right to pursue the non-elected subject matter in one or more divisional or continuation applications should such be necessary.

## **II. Objection to Specification**

### **Embedded Hyperlinks**

The Examiner has objected to the disclosure as containing embedded hyperlinks. Applicants have amended the specification to remove these hyperlinks and thus respectfully request withdrawal of the Examiner's objection.

### **Sequence Listing**

The Examiner has noted that the papers which have been scanned in do not contain the entire Sequence Listing.

The complete sequence listing on paper and CD-ROM was filed with the application on October 22, 2001. Please see a copy of the attached postcard and transmittal sheet, which indicates that a 1527 page sequence listing was filed with the application. Please also see the attached copy of the Image File Wrapper on PAIR, which lists a 1527 page Sequence Listing as one of the "AS FILED" documents for 10/22/01.

As a courtesy to the Examiner, in lieu of a new paper copy of the sequence listing, Applicants have submitted with this response a new complete copy of the sequence listing on CD-ROM in accordance with 37 C.F.R. 1.52(e).

**II. Claim Rejections – 35 USC 112, 2nd paragraph**

Claims 55, 60 and 66-72 have been rejected under 35 USC 112, second paragraph, as allegedly being indefinite for reciting “detection of the expression level of a nucleic acid.” As suggested by the Examiner, Applicants have amended claim 55 to recite “determining the expression level of a nucleic acid” for clarity. Dependent claims 67 to 71 have also been amended to be consistent with the language in amended claim 55. Applicants assert that there is no substantive difference between “detecting” and “determining.” Thus, Applicants respectfully assert that the rejection is now moot and request withdrawal of the rejection.

**II. Claim Rejections – 35 USC 112, 1st paragraph, Written Description**

Claims 55, 60 and 66-72 have been rejected under 35 USC 112, first paragraph, as allegedly failing to describe the claimed subject matter in a way that conveys to one of skill that the inventor had possession of the invention. In particular, the Examiner alleges that because the claim recites “a nucleotide sequence” of SEQ ID NO: 4578, it can be interpreted as encompassing the full length of SEQ ID NO: 4578 as well as all fragments at least two nucleotides long and that the specification lacks written description of any nucleotide sequences of SEQ ID NO: 4578 being associated with transplant rejection. In addition, the Examiner also alleges that there is a lack of written description regarding an association of SEQ ID NO: 4758 and its expression level with transplant rejection. The Examiner alleges that Applicants are relying on obviousness to describe the invention.

Applicants respectfully traverse the rejection regarding written description of fragments of SEQ ID NO: 4758. However, in the interests of expediting prosecution, Applicants have amended the claims to recite a nucleic acid comprising SEQ ID NO: 4758. Applicants thus respectfully assert that the rejection regarding written description of fragments of SEQ ID NO: 4758 is moot.

Applicants also traverse the Examiner’s rejection regarding written description of an association between SEQ ID NO: 4758 and its expression level with transplant rejection. The Examiner appears to be suggesting that the written description requirements include a

demonstration that the claimed invention works. This is simply not the law. In order to satisfy the written description requirements, all that is required is that each claim limitation be either expressly, implicitly, or inherently supported in the specification. MPEP §2163(II)(A)(3)(b). The written description requirements are satisfied for the pending claims.

As filed, the specification provides explicit description of each and every limitation of the claims. This description begins in the Summary of the Invention section, which describes the invention as being directed to methods of diagnosing or monitoring diseases by obtaining leukocyte samples and detecting expression of a diagnostic nucleotide set (page 8, paragraphs 31 to 35). The contents of these diagnostic nucleotide sets are described on page 5, paragraph 15, as having “at least one oligonucleotide wherein the oligonucleotide has a sequence selected from those *sequences listed in Table 2, Table 3, or the Sequence Listing* which is differentially expressed in leukocytes in an individual with at least one disease criterion for a *disease selected from Table 1* as compared to leukocytes from an individual without at least one disease criterion.” Table 1 (p. 183) lists several diseases, including transplant rejection.

Given this description in the Summary of the Invention section, any person of skill, for that matter, any reader of the specification, would understand that the method of the invention involves detection of the expression of various nucleic acids to diagnose or monitor transplant rejection. By further referring to Tables 2, 3, and the Sequence Listing, one of skill would then understand which nucleic acids are detected in methods of this invention. The nucleic acid at which the present claims are directed, SEQ ID NO: 4758, is identified in the specification in two ways. The Sequence Listing and Table 8 (p. 494) identify various 50-mer sequences, including SEQ NO: 4758. In addition, Table 2 (p. 197) lists various nucleic acids identified using data mining as being differentially expressed in leukocytes, including the natural killer cell receptor. SEQ ID NO: 4758 falls within the nucleotide sequence of the natural killer cell receptor; therefore the natural killer cell receptor sequence comprises SEQ ID NO:4758.

Thus, given these descriptions in the specification, one of skill would readily have recognized that Applicants had possession of the claimed invention. The specification describes all limitations of the pending claims. As such, the claims meet the requirements of 35 USC 112, first

paragraph. In view of the above, Applicants thus respectfully request that the Examiner withdraw his rejection of the claims.


### CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. **506612000100**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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